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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,988	02/03/2006	Gary Michael Ksander	PC/4-33209A	6747
75/074	75/074	07/08/2008		
NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC. 400 TECHNOLOGY SQUARE CAMBRIDGE, MA 02139				
EXAMINER				
BARKER, MICHAEL P				
ART UNIT		PAPER NUMBER		
1626				
MAIL DATE		DELIVERY MODE		
07/08/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/556,988

Applicant(s)

KSANDER ET AL.

Examiner

MICHAEL P. BARKER

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 14-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 22-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-893)
Paper No(s)/Mail Date 05/04/2008
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-27 are pending in this Application.

Information Disclosure Statement

The information disclosure statement filed 05/04/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Response to Remarks

Applicant's election, in the reply filed 04/17/2008, of Invention I and species election of Example 4 at p. 45 and 46 of the Specification is acknowledged. Applicant's election was made without traverse, though Applicant argues that the Examiner has not shown an undue burden of searching both Invention I and Invention II. This argument is not persuasive, as the restriction was made based on a lack of unity under PCT Rules 13.1 and 13.2, neither of which discuss undue search burden.

Applicant's elected species is allowable. Thus, per MPEP 803.02, the examination of the Markush-type claim is extended until prior art is found which anticipates or renders the Markush-type claim obvious with respect to a nonelected species. The Markush-type claim will be rejected, *infra*, and claims to the nonelected species will be held withdrawn from further consideration. In this case, **Claims 14-21** are withdrawn from further consideration.

Claim Rejections - 35 USC § 103

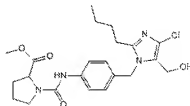
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

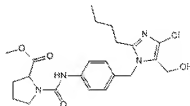
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-13 and **22-27** are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,045,540, issued 09/03/1991.



The '540 patent discloses the following compound: , at col.

22, Example 18, 1-[[[4-[[2-butyl-4-chloro-5-(hydroxymethyl)-1H-imidazol-1-yl]methyl]phenyl]amino]carbonyl]-2-pyrrolidinecarboxylic acid methyl ester. This compound is specifically excluded from the instant claims via a proviso at Claim 1, stating **W** is not 2-butyl-4-chloro-5-hydroxymethylimidazol-1-yl, when **Z** is a bond, **p** is 1, **Q** is a bond, **X₂** is -NR₁₀- in which **R₁₀** is H, and **X₁** is located at the 4-position. However, the '540 compound still renders

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Applicant's Markush-type claim obvious, as it reads upon 1-[[[4-[[2-propyl-4-chloro-5-(hydroxymethyl)-1H-imidazol-1-yl]methyl]phenyl]amino]carbonyl]-2-pyrrolidinecarboxylic acid methyl ester, which is encompassed by the instant Markush-type claim, differing from the '540 compound only by the subtraction of a methylene group. The '540 patent encompasses a substitution of propyl for butyl at the 2-position of the imidazole ring (see col. 4, definition of R²), which suggests that both the 2-butyl and 2-propyl substituted imidazoles would produce similarly reactive compounds. In the case of the '540 patent, similarly reactive compounds would indicate those which are antagonistic as against angiotensin II. Thus, aside from the explicit direction to substitute butyl for propyl in col. 4 of the '540 patent, the motivation to produce the 2-propyl substituted imidazole derives from the desire to produce other angiotensin II antagonists. Many cases have considered the adjacent homologues as obvious variants over each other. For instance, *In re Henze* notes that chemists knowing the properties of one member of a series would, in general, know what to expect in adjacent members, since characteristics normally possessed by members of homologous series are principally the same. 85 USPQ 261, 263 and 265 (CCPA 1950).

Since the issuance of the '540 patent, there is a great deal of literature linking angiotensin antagonists to PPAR agonists, see for example Ernsberger, et al. "Metabolic actions of angiotensin receptor antagonists: PPAR- γ agonist actions or a class effect?", *Current Opinion in Pharmacology*, Vol. 7, pp. 140-5 (2007). Thus, in light of the connection between angiotensin II antagonism and PPAR agonism and the expectation that structurally homologous compound possess similar pharmacological properties, it appears obvious that the '540 compound would be

useful in the treatment of PPAR mediated diseases. Also, the '540 patent specifically discloses pharmaceutical compositions as well as treating heart failure, hypertension, and glaucoma.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 27 recites the limitation "The pharmaceutical composition according to Claim 25. . .". There is insufficient antecedent basis for this limitation in the claim, since Claim 25 is drawn to a method, not a composition.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael P. Barker whose telephone number is (571) 272-4341. The examiner can normally be reached on Monday-Friday 8:00 AM- 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699. The unofficial fax phone for this group are (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is viable through Private PAIR only. For more information about the PAIR system,

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see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael P Barker/
Examiner, Art Unit 1626

/Kamal A Saeed, Ph.D./
Primary Examiner, Art Unit 1626